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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,704	10/29/2001	Dwight Sherod Walker	PU3682USW	4332
23347	7590	09/03/2004	EXAMINER	
DAVID J LEVY, CORPORATE INTELLECTUAL PROPERTY GLAXOSMITHKLINE FIVE MOORE DR., PO BOX 13398 RESEARCH TRIANGLE PARK, NC 27709-3398			GAKH, YELENA G	
			ART UNIT	PAPER NUMBER
			1743	

DATE MAILED: 09/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	S.C.
	10/009,704	WALKER ET AL.	
	Examiner	Art Unit	
	Yelena G. Gakh, Ph.D.	1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 30 August 2004.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 10-25 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 10-25 and 30 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 29 October 2001 is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some *
 - c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ . |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>07/19/04</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ . |

DETAILED ACTION

1. RCE and Amendment filed on 07/29/04 are acknowledged. 1-9 and 26-29 are cancelled without prejudice. Claims 10-25 and 30 are pending in the application.

Response to Amendment

2. The amendment of the specification appears to rely on the specification as originally filed, rather than the amended specification filed 12/22/2003. Clarification is required.

The rejection of the pending claims over the prior art is withdrawn in light of cancellation of the claims.

The objection to the specification and rejections of the pending claims under 35 U.S.C. 112, first and second paragraphs are not overcome by the amendment and stay as they were established in the previous Office actions.

Specification

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The specification is objected to as not written in such clear and exact terms as to enable any routineer in the art to practice the invention in its best mode. The specification discloses measuring the absorption spectrum of the cryogenic liquid using IR spectroscopy and obtaining the reference cryogenic liquid absorption spectrum. The specification further refers to the IR spectra having (or, as was proposed later, ‘corresponding to’) a reference energy (page 2, line 25). As it was indicated in the previous Office actions, the expression “absorption spectrum having a reference energy” is not proper. How can the spectrum have absorption energy? By definition (Merriam-Webster On-line Dictionary), “**electromagnetic spectrum** is the entire

range of wavelengths or frequencies of electromagnetic radiation extending from gamma rays to the longest radio waves and including visible light". Each wavelength or frequency corresponds to specific absorption energy. Therefore, the expression "absorption spectrum having a reference energy" does not have any sense, since the spectrum itself is a continuum of variable energies.

It is further unclear, how IR spectrum of the impurity alone can be measured, when the impurity is unknown and therefore is not available in a pure state.

Formula given on page 4 is completely unapparent. Is this the formula deduced by the inventors, or is it a known formula? If this is a known formula, the corresponding reference, which describes it, is required. In description of the system of the invention on the same page very clear and correct terms are used for describing the same subject matter, i.e. measuring "absorption intensities" in IR spectra of the reference cryogenic liquid, reference impurity and cryogenic sample having this impurity.

The examiner would like to emphasize again that the absorption energy of molecules (not the spectrum!) and intensity (or power) of light are not synonyms; they are defined clearly and unambiguously in the art, see e.g. "Fundamentals of Spectrophotometry" in "Quantitative Chemical Analysis" by Harris. It is well known to any routineer in the art that absorption energies define the origin of the molecule, specifically IR absorption energies define vibration states of the molecular functional groups, and have nothing to do with the concentration of the compound; at the same time intensities of the absorption lines (or changes in the light power, or transmittance) define the concentration of the compound. It is completely unclear, how dividing a frequency of one compound over the frequency of the other compound allows determining the concentration of the first one in the second? Even less it is clear, how the concentration of one compound in another compound can be determined from the spectra of two pure compounds, with 100% concentration of each of them?

Further, chemical compounds, i.e. contaminants or impurities, cannot be defined by their vibration energies (not mentioning incorrectness of such terminology) (page 6). Vibration energies are associated with specific bonds (e.g. C=O, or C-C, or C=C bonds), which can belong to numerous compounds. It is not clear, how any routineer in the art can determine, which compounds are considered impurities in the instant method by defining vibration energies of their bonds. It is only possible to determine, which bonds are present in the molecules. Such

description does not give a clear and apparent description of the potential contaminants and is inappropriate for the disclosure, which, as it has already been stated lacks clarity in general.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 10-25 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Nature of the Invention

Invention is directed to identifying and quantifying impurities in cryogenic liquid by measuring NIR spectrum of cryogenic liquid, “corresponding to a first reference energy”; measuring NIR spectrum of a “pure” impurity, and again measuring the absorption spectrum of the cryogenic liquid sample; comparing the absorption spectra of these liquids, **confirming** the presence of “said cryogenic liquid sample absorption spectrum associated with said impurity, said sample absorption spectrum associated with said impurity corresponding to a second reference energy”, and determining the concentration as the logarithm of the ratio of the second reference absorption energy to the first reference absorption energy. The language of the disclosure raises the question as to what the essence of the invention is.

As it was indicated above, absorption spectrum cannot be associated with a reference absorption energy, since by definition, “**electromagnetic spectrum** is the *entire range* of wavelengths or frequencies of electromagnetic radiation extending from gamma rays to the longest radio waves and including visible light”, with each wavelength or frequency

corresponding to specific absorption energy. Thus, the terminology of the claims contradicts the only possible and accepted terminology and makes the nature of the invention unclear.

Claims 10 and 18 recite a method for identifying impurities, and at the same time recite a step for measuring absorption spectrum of the “pure” impurity. If it is possible to measure the absorption spectrum of the “pure” impurity, then why should it be identified?

The first and the third steps of the method recite measuring the absorption spectrum of the cryogenic liquid and a cryogenic liquid sample. What is the difference between these two? If this is the same cryogenic liquid, then the absorption spectra will be the same, and the first cannot be used as a reference spectrum.

The mathematical expression relating the concentration of the impurity to the logarithm of the ratio of two “reference absorption energies” is the least clear part of the disclosure. The examiner does not recall any reference on IR spectroscopy with such relation. Corresponding reference is required.

The State of the Prior Art and the Level of Predictability in the Art

Moulson (Nuclear Instruments) teaches “monitoring of dopant and impurity concentrations in liquid argon by infrared spectroscopy” (Title) by measuring IR spectra of cryogenic argon (Figure 2), an impurity (volatile organic compound having CH bond, ethylene) alone (Figure 3a) and impurity in the cryogenic liquid (Figure 3b) in a spectrum range 400-4000 cm^{-1} (2500-250 nm) (Figures 1-3) in a flow cell with a pressure drop between 0.85-1.05 bar (~ lb/in²) (page 278, right column) and confirming the presence of the impurity by comparing the spectrum with the reference spectra of pure argon and ethylene. “The cell was originally designed to be combined with a detector used to study the ionization characteristics and electron mobilities of doped liquid argon solutions [7], so that IR analysis of the solutions could be performed *in situ*” (i.e. on-line) (pages 277-278). Moulson teaches all the steps of the claims using conventional terminology of the art, i.e. reciting signal intensities in the spectra, rather than “absorption energies”. He does not calculate concentration of the impurity as logarithm of the ratio of the second and first reference absorption energies. As it was indicated above, none of the textbooks on spectroscopy known to the examiner refers to such expression. The only

expression that uses logarithm of the ratio of intensities (or power) of the light to find concentration of the absorbing compound is a well-known Beer's law. As it was mentioned before, the terms "absorption energy of the molecules" and "intensity (or power) of light" are not synonyms. The absorption energies define the origin of the molecule, specifically IR absorption energies define vibration states of the molecular functional groups, and therefore are specific for specific functional groups; they have nothing to do with the concentration of the compound. The concentration of the compound is determined by the intensities of the absorption lines (or changes in the light power, or transmittance) of the compound. The prior art does not teach or predict quantitative analysis based on IR spectroscopy using the formula recited in the claims.

The disclosure does not teach or give any guidance of how to measure named absorption energies, since it is unclear, what they are; less so the disclosure teaches how to use them for the calculating the concentration of the compound.

Claims 16, 24 and 30 recite compounds defined by their vibration frequencies in nm. As it was indicated above, vibration energies are associated with specific bonds (e.g. C=O, or C-C, or C=C bonds), which can belong to numerous compounds. It is not clear, how any routineer in the art can determine, which compounds are considered impurities in the instant method by defining vibration energies of their bonds. It is only possible to determine, which bonds are present in the molecules. Such description does not give a clear and apparent description of the potential contaminants and is inappropriate for the disclosure, which, as it has already been stated lacks clarity in general.

The Existence of Working Examples

The working examples refer to measuring "absorption intensities" in IR spectra of the reference cryogenic liquid, reference impurity and cryogenic sample having this impurity and determining the amount of the impurity from these intensities. This is a conventional way of detecting impurities in the sample using IR spectroscopy by subtracting background spectrum of the reference compound. It has nothing to do with the expression disclosed in the specification and recited in the claims. There are no working examples for the subject matter recited in the pending claims.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 10-25 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is already indicated that the expression “absorption spectra corresponding to a reference energy”, recited in claims 10 and 18 is technically incorrect and does not have any sense.

It is further unclear, which cryogenic liquid is meant in the first and the third steps of the method. If this is the same cryogenic liquid, then how it can be used as a reference in the first step, and as an analyte in the third step?

In the second step, the impurity alone (i.e. pure “impurity) is being measured. If the impurity is not known (i.e. is not identified), how is it possible to perform this step?

It is not apparent, what the whole phrase “confirming the presence of said cryogenic liquid sample absorption spectrum associated with said impurity” might mean. Why should be the presence of the absorption spectrum of the cryogenic liquid confirmed? If the absorption spectrum is measured, then its presence does not need to be confirmed – otherwise it was not measured. The expression is very confusing.

The mathematical expression in claims 10 and 18 is so unclear, that the examiner requests any reference, which provides such expression for calculating concentrations of the compounds from IR spectra.

The terminology used by the Applicants in the specification and claims completely contradicts accepted terminology in the art and makes the disclosure unclear, indefinite, and confusing.

Claims 16, 24 and 30 recite “a material having a vibration energy in the range of approximately 1000 nm to 250 nm”. First, this is not a correct technical definition. The material can comprise molecules having bonds with vibration energies of the range recited in the claims. Second, chemical compounds, i.e. contaminates or impurities, cannot be defined by their vibration energies. Vibration energies are associated with specific bonds (e.g. C=O, or C-C, or

C=C bonds), which can belong to numerous compounds. It is not clear, how any routineer in the art can determine, which compounds are considered impurities in the instant method by defining vibration energies of their bonds. It is only possible to determine, which bonds are present in the molecules. Such description does not give a clear and apparent description of the potential contaminants and is inappropriate for a disclosure, which, as it has already been stated lacks clarity in general

Response to Arguments

9. Applicant's arguments filed 07/19/04 have been fully considered but they are not persuasive.

First, the examiner does not quite comprehend the whole statement related to the examiner's objections to the specification: "in summary, the Office alleges that invention cannot be a single infrared (IR) absorption spectrum for a compound and that such values cannot be employed to determine the concentration of a compound". It is unclear, what does the whole phrase mean? Does it say that the invention is "a single infrared (IR) absorption spectrum for a compound"? The examiner would like to ask the Applicants to indicate more clearly, which single IR spectrum of the compound is disclosed as the invention. Also, it is not clear, which "*such values* cannot be employed to determine the concentration of a compound"? Such values of what? Contrary to the Applicant's statement, the examiner could not assert what the Applicants indicate as the essence of the examiner's objection to the specification, because she just does not understand such interpretation of her objection.

The next phrase, "in the near-infrared region, absorption spectra may correspond to energies of various substances" is completely unclear. What does the statement mean? What are "the energies of various compounds"? Compounds have Gibbs's energies of formation. If these are the energies that are determined by the Applicants from NIR spectra, this is something really new. The Applicant's reference to the basic text of Ciurczak concerning "principles of NIR spectroscopy" does not shed any light to the Applicant's argumentation, as the text basically describes elementary principles of NIR spectroscopy, which can be found in any college physical

chemistry textbook, and which puts into formulas what the examiner previously described in words.

Further, the Applicants refer to near-infrared spectroscopy, with the emphasis on the word “near”. It is not clear, what this may change in the examiner’s and Applicant’s argumentation. The whole infrared region of the spectrum is conventionally divided into three (sometimes just two) regions - near-infrared, mid-infrared and far-infrared, with various frequency limits given for near-infrared region in different sources, e.g. 780-2500 nm (New & Features), 770-1400 nm (The Infrared Spectrum). Therefore, the term “near-infrared” just gives a more specific definition of the region of infrared spectrum. It is not clear, how referring to the near infrared region of the spectrum can address the rejection of the pending claims under 35 U.S.C. 112, first paragraph as un-enabled? The Applicants did not demonstrate, how they obtain the concentration of a compound through the ratios of two reference energies. What is shown in Figure 5 is changing the **intensity** of the signal **at the same frequency**, which is conventionally used for determining concentration of a compound. If the Applicants wish to convincingly demonstrate enablement of the claimed method, they are expected to present any reference, which discloses the same approach to quantitative NIR analysis through the “first and second reference energies of the spectrum”.

While the arguments regarding rejections of the claims over the prior art are moot in view of the amendment, the examiner would like to notice, that the invention, if disclosed using the proper terminology, is completely covered by Moulson’s reference, which specifically and unambiguously discloses a method for on-line (in-situ) NIR (near infrared) detection of the impurities in cryogenic liquids in a flow cell. The fact, that for the specific experiment on-line flow-cell was used for off-line analysis for the purpose of initial conducting the experiments in a simpler environment, does not change the anticipatory character of Moulson’s reference and does not make it un-enabling, contrary to the Applicant’s arguments.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yelena G. Gakh, Ph.D. whose telephone number is (571) 272-1257. The examiner can normally be reached on 9:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill A. Warden can be reached on (571) 272-1267. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Yelena G. Gakh
8/30/04

A handwritten signature in black ink, appearing to read "Yelena Gakh".